PRODUCTION OF ATTENUATED RESPIRATORY SYNCYTIAL VIRUS VACCINES INVOLVING MODIFICATION OF M2 ORF2

ABSTRACT OF THE DISCLOSURE

Recombinant respiratory syncytial virus (RSV) are provided in which expression of the second translational open reading frame encoded by the M2 gene (M2ORF2) is reduced or ablated to yield novel RSV vaccine candidates. Expression of M2 ORF2 is reduced or ablated by modifying a recombinant RSV genome or antigenome to incorporate a frame shift mutation, or one or more stop codons in M2 ORF2. Alternatively, M2 ORF2 is deleted in whole or in part to render the M2-2 protein partially or entirely non-functional or to disrupt its expression altogether. M2 ORF2 deletion and knock out mutants possess highly desirable phenotypic characteristics for vaccine development. These changes specify one or more desired phenotypic changes in the resulting virus or subviral particle. Vaccine candidates are generated that show a change in mRNA transcription, genomic or antigenomic RNA replication, viral growth characteristics, viral antigen expression, viral plaque size, and/or a change in cytopathogenicity. In addition, M2-2 knock out or deletion virus exhibits increased levels of synthesis of viral proteins in cell culture, providing an enriched source of viral antigen or protein for purification and use as a noninfectious subunit vaccine.